BIND 2

Brain INvolvement in Dystrophinopathies (BIND): Deep Functional Phenotyping of Duchenne Muscular Dystrophy and Becker Muscular Dystrophy Patients (WP5 and WP6) Part 2: a Neurobehavioural and MRI Study

Hub Summary

The objective of this study is to understand the relationship between DMD and BMD brain comorbidities, and the location of the gene mutation which causes the disease.

The investigators will recruit both patients who have completed a related online study (ClinicalTrials.gov Identifier NCT04583917) and patients directly recruited from participating clinics or research settings. These patients will undergo a structured cognitive and neurobehavioural assessment. A subgroup of patients assessed in the research setting will be invited to also attend a second visit involving a magnetic resonance imaging (MRI) scan of the brain.

The investigators aim to recruit 80 participants in the UK and the number of participants in the remaining countries will be 190 patients.

Study Number: NCT04668716

Description by Great Ormond Street Hospital for Children NHS Foundation Trust

Intellectual disability and neurobehavioural comorbidities affect at least 50% of the individuals with Duchenne muscular dystrophy (DMD) which, although a rare genetic disease, is the most common form of muscular dystrophy in childhood. Several studies have documented that 25% of the DMD population has intellectual disability with recent studies suggesting that autism and clinically relevant hyperactivity affects 20% and 25% of DMD boys respectively. A milder allelic variant, named Becker muscular dystrophy (BMD), has similar prevalence in the population and is also associated with variable degrees of central nervous system (CNS) comorbidities, which however have been less well defined.

We will address this knowledge gap in a large multicentre study funded by the European Commission H2020 programme, involving 6 countries (Denmark; The Netherlands; France; Spain; Italy and UK) with the largest European neuromuscular centres and advocacy groups. The aim will be to study the neurobehavioural aspects of DMD and BMD as well as their correlation to the genotype.

This study will involve male participants with DMD aged 5-17 years and with BMD aged 5-50 years, who will complete a battery of cognitive and behavioural assessments. The objective of this study is to deep phenotype a cohort of 270 individuals with DMD and BMD, focussing on the cognitive and neurobehavioural aspects of these conditions. A sub-groups of patients will also undergo magnetic resonance imaging to investigate brain structure, volumetric features, perfusion, functional connectivity and metabolism. This information will then be correlated to the location of the underlying DMD gene mutation. The brain imaging part is also going to involve age and sex-matched controls.

While there have been major improvement on the definition of the genetic basis of the skeletal aspects of dystrophinopathies and their correlation to the DMD genotype, our knowledge on the spectrum of lifespan CNS comorbidities and the precise genotype / phenotype correlations in patients with different DMD mutations is still limited. A study looking into the association between different dystrophin isoforms and different CNS manifestations would therefore offer a unique opportunity to unravel the role of specific dystrophin isoforms and the associated circuitries in brain function.

Can I take part?

Trial Status
Fully recruited

UK Locations
London - GOSH, Fully recruited, Newcastle, Fully recruited

Trial Sponsor
Great Ormond Street Hospital for Children NHS Foundation Trust

Age
5-17

Mutation Specific
Non-mutation specific therapies

Muscle Biopsy
No Muscle Biopsy Required

MRI
No

Recruitment Target
80

Ambulatory
Ambulant and non-ambulant

Therapeutic Category
Observational

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Inclusion Criteria

- Male
- age 5-17 years
- genetically-proven diagnosis of DMD
- genetic mutation that abrogates expression of Dp427 alone (assigned in DMD Group 1: Dp427-/Dp140+) or both Dp427 and Dp140 (assigned to DMD Group 2: Dp427-/Dp140-); or all isoforms (assigned to DMD group 3)

For MRI controls:

- Male
- age 5-50 years

Exclusion Criteria

- Lack of a molecular diagnosis of DMD or BMD
- Mutation falls outside the regions of interest
- A severe co-morbidity or planned surgical intervention within 6 months from the study which could interfere with the well-being of the participant

For MRI controls:

- any muscle disease
- a brain disorder (such as severe brain concussion in past history, congenital brain anomalies, epilepsy)

General exclusion criteria for MRI:

- Claustrophobia
- Pacemakers and defibrillators
- Nerve stimulators
- Intracranial clips
- Intraorbital or intraocular metallic fragments
- Cochlear implants
- Ferromagnetic implants (e.g. thoracic implant for scoliosis)
- Inability to lie supine during less than 45 minutes
- not having a general practitioner
- severe learning disability which will require a general anaesthetic

For contact details and to find out more, please refer to dmdhub.org.

Duchenne UK

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